and 0.87 [0.68, 1.11] vs 0.655 [0.455, 0.944], respectively. **CONCLUSIONS:** This analysis shows the improved survival of patients who received novel therapies as compared to conventional therapies, across the different therapy lines. Additionally, results illustrate the impact of selection bias induced by selective treatment switching, and the need to apply novel approaches as IPCW to make additional adjustments, for which traditional statistical techniques cannot be used for.

PRM16

COMPARING THE USE OF PATIENT-LEVEL DATA TO AN AVERAGE PATIENT PROFILE WITHIN A TYPE 2 DIABETES SIMULATION MODEL

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OBJECTIVES: Despite significant patient heterogeneity and complex treatment pathways, averages are commonly relied upon when defining patient populations and treatment effects within type 2 diabetes modeling. As a result, clinicians may struggle to relate results to the clinical setting. This study compares outcomes when using patient-level and average cohort inputs within a published simulation model, based on the UKPDS68 outcomes equations. **METHODS:** UK patient data (2,251 patients initiating dual therapy) were obtained from The Health Improvement Network (THIN). Simulations, performed over a medium-term horizon of 20 years, utilised either patient-level data, collating outputs over all replications, or average cohort data. The outputs (total costs, benefits and complication rates) were then compared. **RESULTS:** Average baseline characteristics were: age: 63.36 (±11.14) years; HbA1c: 8.39% (±1.23); total cholesterol: 4.18 (±0.92) mmol/L; systolic blood pressure: 135.07 (±14.76) mmHg; weight: 89.85 (±19.01) kg. The mean treatment effect was a reduction in HbA1c of 1.01 (±1.23) %. Over 20 years, fewer macrovascular and microvascular events (-82/1,000 patients) and higher all-cause mortality (+17/1,000 patients) were predicted when using patient-level data compared to the average profile. Differences in the frequency and timing of deaths were driven primarily by variation in age and led to fewer estimated life-years (-0.66), quality-adjusted life-years (QALYs; -0.59) and costs (-£551) per patient. Patients estimated to have lower costs and higher QALYs than those associated with the average profile were younger, with higher HbA1c and cholesterol but lower blood pressure at baseline. **CONCLUSIONS:** Modelling results differ depending on the use of patient-level or average cohort model inputs. Patient-level data may provide insight into the type of patients in whom therapy is likely to be most beneficial. Furthermore, it enables the accurate simulation of correlation between patient characteristics and treatment effect, which are rarely accounted for as part of a standard probabilistic sensitivity analysis.

PRM17

QUANTIFYING NONLINEAR EFFECTS IN STOCHASTIC MARKOV SIMULATION USING UKPDS 68 AND UKPDS 82 EQUATIONS IN TYPE 2 DIABETES MODELING ANALYSIS WITH THE IMS CORE DIABETES MODEL (CDM)

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OBJECTIVES: Previous studies have demonstrated incorporating parameter sampling (PS) is crucial to capture nonlinear effects (NE) in cost effectiveness modeling. NE are, among other causes, driven by the degree through which the symmetric sampling of a risk factor is translated into non-symmetrically distributed probabilities generated by the applied risk equations (RE). This study sought to assess degree by which the incorporation of NE through PS alters event rate predictions from the UKPDS 82 (UK82) and UKPDS 68 (UK68) RE in a set of selected validation studies conducted with the CDM. **METHODS:** A total of 50 validation simulations were performed to data from ACCORD, ADVANCE, VADT, ASPEN, DCCT and UKPDS. Simulations mirroring cohort baseline characteristics of each of the trials were conducted with and without PS using UK68 and UK82 REs. Predicted versus observed macrovascular (MAC) and microvascular (MIC) complications and all cause mortality (ACM) were assessed using the coefficient of determination (R2) goodness of fit measure. **RESULTS:** When the CDM was run without PS, validation studies produced an R2 statistic of 0.898 using UK68 and 0.853 using UK82 RE. This compared to R2 statistics of 0.876 and 0.791 in analysis with PS for UK68 and UK 82 REs, respectively. Overall, PS caused end point predictions for MAC, MIC and ACM to increase. Internal validations against UKPDS 80 demonstrated that PS increased event rate predictions for myocardial infarction (MI), stroke, MIC and ACM by 4.4%, 21.5%, 19% and 16.4% when UK68 RE were applied and 26.3%, 64.7%, 14.9% and 34.8% with UK82 RE, respectively. **CONCLUSIONS:** The findings from this study have shown that external validity declined with PS in simulations using UK68 RE and UK82 RE. The degree by which PS increased end point predictions was considerable stronger in UK82 RE predictions for MAC and ACM but lower for MIC.

PRM18

INVERSE PROBABILITY OF CENSORING WEIGHTED ANALYSIS TO ADJUST THE TREATMENT EFFECT ON OVERALL SURVIVAL FOR SUBSEQUENT THERAPY: A CASE STUDY IN A CLINICAL TRIAL IN MULTIPLE MYELOMA

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OBJECTIVES: ITT-analyses of oncology trials tend to underestimate the treatment effect on overall survival, due to the impact of subsequent therapy. Inverse probability of censoring weighted analysis (IPCW) was explored to estimate an adjusted treatment effect on OS in VISTA, a phase III randomized clinical trial comparing melphalan and prednisone with or without bortezomib (VMP vs MP) in previously untreated multiple myeloma patients ineligible for stem cell transplantation. **METHODS:** The IPCW consisted of 2 steps. First, time-varying weights were estimated using multivariate logistic regression, including age, gender, stage, M-protein type, creatinine-clearance as baseline covariates and M-protein as time-varying covariate. In a second step, these time-dependent weights were incorporated in a proportional hazards model, including the same baseline characteristics, with patients censored at initiation of subsequent therapy. **RESULTS:** 338/344 patients received up to nine 6-week cycles of VMP or MP respectively, with median follow-up of 44.2 months. 68% of MP-patients received subsequently therapy, compared to 58% in the VMP-arm. Age<75, creatinine-clearance 30-60ml/min, stage III, and increasing M-protein measures over time were additional drivers for treatment-switching. The IPCW-approach generated an adjusted hazard ratio of 0.584 [0.406, 0.839], compared to the ITT-estimate of 0.704 [0.576, 0.860]. **CONCLUSIONS:** In oncology, particularly in early line treatment, it is common that patients receive subsequent treatment lines. This typically happens more frequently and earlier in the comparator arm, which may bias the estimate for the treatment effect on OS. The IPCW-approach was explored to adjust for this bias, which resulted in an increased estimate of the treatment-effect on OS of VMP vs MP, compared to the original ITT-analysis. With overall survival being a key input in economic evaluation, estimating the accurate effect on OS is key. Employing this type of approaches may result in more accurate cost effectiveness results and thus more consistent/appropriate Health Technology Assessment recommendations.

PRM19

SHARING OF INFORMATION ACROSS STUDIES TO INFORM CHOICE OF FUNCTIONAL FORM WHEN CONDUCTING PARAMETRIC SURVIVAL ANALYSIS

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OBJECTIVES: To explore the sharing of information across multiple studies in order to inform the choice of functional form when conducting parametric survival analysis. **METHODS:** A set of four clinical trials in advanced soft tissue sarcoma were identified from a published systematic review. Individual patient data for overall survival were estimated from digitised Kaplan-Meier curves using a published algorithm. A range of parametric survival models (exponential, Weibull, Gompertz, log-normal, log-logistic, Gamma and Generalised Gamma) were fitted. Two approaches were explored for identifying the preferred parametric model: (i) selecting models independently for each study (ii) selecting a common model across all the studies. Models were selected using the Bayesian Information Criterion (BIC). For approach (ii) a single BIC statistic was calculated by summing the components of the BIC (n, k and ln (L)) across studies. Estimates of mean survival were derived for each model and a bootstrap analysis was conducted to estimate both the uncertainty in model selection and the variance in mean survival estimates. **RESULTS:** Independent selection led to different functional forms being selected for each study with considerable uncertainty regarding the choice of model (the bootstrap estimation for the probability that the optimum model had been selected varied between 16 to 84% across studies). The choice of model influenced mean survival predictions. Selecting a common model across studies was found to reduce the uncertainty in model selection and variance of the estimated mean survival (by up to 65%) compared to selecting models independently. **CONCLUSIONS:** Use of multiple studies to inform choice of functional form can improve the efficiency of survival estimates and hence reduce uncertainty of cost-effectiveness estimates. Given the considerable uncertainty in selecting survival models within individual studies, it may be reasonable to treat information on functional form as exchangeable between studies and to 'borrow' strength across studies.

PRM20

PREDICTIVE MODELING TO ASSESS PREDICTORS OF TREATMENT SUCCESS AND FAILURE AMONG COMBINATION STATIN THERAPY PATIENTS

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OBJECTIVES: Combination statin therapy may help to further lower low-density lipoprotein cholesterol (LDL-C) better than monotherapy alone. The objective of this study was to apply predictive modeling methodology to determine the predictors of success and failure in achieving LDL-C goals after combination statin-fibrate therapy in patients diagnosed with hypertriglyceridemia (HTG). **METHODS:** A large claims database was used to identify patients initiating a fibrate between January 2011 and December 2011 (index date). Diagnosis of HTG and the use of statins were confirmed within 6 months before the index date. A total of 622 patients were selected for the current analysis. Patients were categorized into very high risk, high risk, moderate risk, and low risk groups. Logistic regression and two-group discriminant analysis models based on 17 potential predictors for treatment success or failure were constructed. **RESULTS:** At index, the median triglyceride (TG) level among all patients was 95.5 mg/dL, LDL-C level was 92 mg/dL, and high-density lipoprotein (HDL) was 40 mg/dL. The mean age was 54 years. Two predictors were associated with combination statin-fibrate treatment success or failure and accounted for 5.3% of variance between groups. Low HDL (defined as <40 mg/dL) (OR=0.35; 95% CI, 0.20-0.59) and peripheral arterial disease (OR=0.10; 95% CI, 0.02-0.38) were significantly associated with treatment failure. Low HDL variable was the key discriminator. **CONCLUSIONS:** Analytic insights enabled by predictive models may help researchers gain information on discriminating factors about certain target treatment groups and drug classes. A set of key predictors may suggest opportunities to understand and predict treatment success and failure of targeted groups and/or drug classes. These predictors may be useful in developing treatment strategies that will optimize outcomes.

PRM21

PREDICTIVE MODELLING FOR OPTIMAL TARGET POPULATION AND REAL-WORLD STUDY DESIGN: AN EXAMPLE IN MOTHER-TO-CHILD TRANSMISSION OF HIV

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